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U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

**TRANSMITTAL LETTER TO THE UNITED STATES
DESIGNATED/ELECTED OFFICE (DO/EO/US)
CONCERNING A FILING UNDER 35 U.S.C. 371**

ATTORNEY'S DOCKET NUMBER
08291-670001

U.S. APPLICATION NO. (If Known, see 37 CFR
1.51)

09/720941

INTERNATIONAL APPLICATION NO
PCT/GB99/01963

INTERNATIONAL FILING DATE
23 June 1999

PRIORITY DATE CLAIMED
2 July 1998

TITLE OF INVENTION
INHALATION OF AEROSOL ACTIVES

APPLICANT(S) FOR DO/EO/US

Rodney Thomas FOX, Neale HARRISON, John Farrell HUGHES, Duncan Roger HARPER, Lindsey Faye WHITMORE and Karen Louis JERRIM

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371
3. ☒ This is an express request to promptly begin national examination procedures (35 U.S.C. 371(f)).
4. ☐ The US has been elected by the expiration of 19 months from the priority date (PCT Article 31).
5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
 - a. ☐ is attached hereto (required only if not communicated by the International Bureau).
 - b. ☒ has been communicated by the International Bureau.
 - c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☐ An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
 - a. ☐ are attached hereto (required only if not communicated by the International Bureau).
 - b. ☐ have been communicated by the International Bureau.
 - c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
 - d. ☒ have not been made and will not be made
8. ☐ An English language translation of amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)) (UNSIGNED).
10. ☐ An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5))

Items 11 to 16 below concern other documents or information included:

11. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98
12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☒ A **FIRST** preliminary amendment
☐ A **SECOND** or **SUBSEQUENT** preliminary amendment
14. ☐ A substitute specification.
15. ☐ A change of power of attorney and/or address letter
16. ☒ Other items or information:
 - ☒ PCT Notification of Transmittal of the International Preliminary Examination Report dated 9 October 2000.
 - ☐
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CERTIFICATE OF MAILING BY EXPRESS MAIL

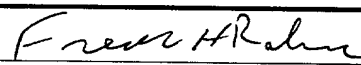
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I hereby certify under 37 CFR §1.10 that this correspondence is being deposited with the United States Postal Service as Express Mail Post Office to Addressee with sufficient postage on the date indicated below and is addressed to the Commissioner for Patents Washington, D.C. 20231

January 2, 2001
Date of Deposit

Francine Bobb
Signature

Francine Bobb
Typed Name of
Person Signing

U.S. APPLICATION NO. (IF KNOWN) 09/720941		INTERNATIONAL APPLICATION NO. PCT/GB99/01963		ATTORNEY'S DOCKET NUMBER 08291-670001																															
17. <input type="checkbox"/> The following fees are submitted: Basic National Fee (37 CFR 1.492(a)(1)-(5)): Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO..... \$1000 International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO . . . \$860 International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO \$710 International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4) \$690 International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4) \$100 <div style="text-align: right;">ENTER APPROPRIATE BASIC FEE AMOUNT =</div>				CALCULATIONS PTO USE ONLY																															
Surcharge of \$130 for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(e)).				\$860.00																															
<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 20%;">Claims</th> <th style="width: 20%;">Number Filed</th> <th style="width: 20%;">Number Extra</th> <th style="width: 20%;">Rate</th> <th style="width: 20%;"></th> <th style="width: 20%;"></th> </tr> </thead> <tbody> <tr> <td>Total Claims</td> <td>16 - 20 =</td> <td>0</td> <td>x \$18</td> <td>\$0.00</td> <td></td> </tr> <tr> <td>Independent Claims</td> <td>1 - 3 =</td> <td>0</td> <td>x \$80</td> <td>\$0.00</td> <td></td> </tr> <tr> <td colspan="3">MULTIPLE DEPENDENT CLAIMS(S) (if applicable)</td> <td>+ \$270</td> <td>\$0.00</td> <td></td> </tr> <tr> <td colspan="4" style="text-align: right;">TOTAL OF ABOVE CALCULATIONS =</td> <td>\$860.00</td> <td></td> </tr> </tbody> </table>				Claims	Number Filed	Number Extra	Rate			Total Claims	16 - 20 =	0	x \$18	\$0.00		Independent Claims	1 - 3 =	0	x \$80	\$0.00		MULTIPLE DEPENDENT CLAIMS(S) (if applicable)			+ \$270	\$0.00		TOTAL OF ABOVE CALCULATIONS =				\$860.00		\$0.00	
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a. <input checked="" type="checkbox"/> A check in the amount of \$860.00 to cover the above fees is enclosed. b. <input type="checkbox"/> Please charge my Deposit Account No. 06-1050 in the amount of \$0.00 to cover the above fees. A duplicate copy of this sheet is enclosed. c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 06-1050. A duplicate copy of this sheet is enclosed.																																			
NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b) must be filed and granted to restore the application to pending status.																																			
SEND ALL CORRESPONDENCE TO																																			
Frederick H. Rabin FISH & RICHARDSON P.C. 45 Rockefeller Plaza, Suite 2800 New York, NY 10111 (212) 765-5070 phone (212) 258-2291 facsimile Date: <u>2 Jan. 01</u>			<div style="text-align: center;">  SIGNATURE </div> <div style="text-align: center;"> NAME Frederick H. Rabin </div> <div style="text-align: center;"> REGISTRATION NUMBER 24,488 </div>																																

526 Rec'd PCT/PTO 02 JAN 2001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Rodney Thomas FOX et al.
Int'l Appln. No.: PCT/GB99/01963
Int'l Filing Date: 23 June 1999
Title : INHALATION OF AEROSOL ACTIVES

Box: PCT

Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT UNDER 37 C.F.R. § 1.115

Prior to examination of this application, kindly enter the following amendments:

In the Specification:

On page 1, line 2: insert, as a heading:

--Background of the Invention--.

On page 1, after line 18: insert, as a heading:

--Summary of the Invention--.

On page 2, after line 2: insert:

--Brief Description of the Drawings

Figure 1 is a diagrammatic cross section through an aerosol spraying apparatus in accordance with the invention;

Figure 2 is a diagrammatic cross section through the valve assembly of the apparatus of Figure 1;

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January 2, 2001

Date of Deposit

Francisco Robles

Signature

Francisco Robles

Typed or Printed Name of Person Signing Certificate

Figure 3 is a cross section through the actuator insert of the assembly shown in Figure 2;

Figure 4 shows the configuration of the bore of the spraying head shown in Figure 3 when viewed in the direction A;

Figure 5 shows the configuration of the swirl chamber of the spraying head shown in Figure 3 when viewed in the direction B;

Figure 6 illustrates the results obtained in Example 2; and

Figure 7 illustrates the results obtained in Example 3.

Detailed Disclosure--.

On page 5, line 31: change "increase" to --increases--.

On page 8, line 11: change "accompanying drawings, in which:-" to --drawings.--.

On page 8, lines 12-28: delete "Figure 1 is a diagrammatic cross section through an aerosol spraying apparatus in accordance with the invention; Figure 2 is a diagrammatic cross section through the valve assembly of the apparatus of Figure 1; Figure 3 is a cross section through the actuator insert of the assembly shown in Figure 2; Figure 4 shows the configuration of the bore of the spraying head shown in Figure 3 when viewed in the direction A; Figure 5 shows the configuration of the swirl chamber of the spraying head shown in Figure 3 when viewed in the direction B; Figure 6 illustrates the results obtained in Example 2; and Figure 7 illustrates the results obtained in Example.".

On page 10, line 27: change "2" to --two--.

On page 11, line 17: change "L/a" to --L/a--.

On page 11, line 23: change "L/a" to --L/a--.

On page 12, line 15: change "4" to --four--.

On page 12, line 26: change "illustrates" to --illustrate--.

On page 13, line 5: change "iso paraffin" to --isoparaffin--.

On page 13, line 23: change "2" to --two--.

In the Claims:

The claims in this application are as follows:

--1. A method of reducing the inhalation of airborne/respirable particles or droplets having a diameter of less than 10 micrometres, produced by spraying liquid droplets from a spray device, which method comprising imparting a unipolar charge to the liquid droplets by double layer charging during the spraying of the droplets from a spray device, the unipolar charge being at a level such that the droplets have a charge to mass ratio of at least $\pm 1 \times 10^{-4}$ C/kg, whereby at least 10% by volume of the airborne respirable particles or droplets having a diameter of less than 10 micrometres in the vicinity of the mouth, nose or upper respiratory tract do not enter the lungs.

2. A method as claimed in claim 1 wherein at least 25% by volume of the airborne respirable particles or droplets having a diameter of less than 10 micrometres in the vicinity of the mouth, nose or upper respiratory tract do not enter the lungs.

3. A method as claimed in claim 1 wherein at least 40% by volume of the airborne respirable particles or droplets having a diameter of less than 10 micrometres in the vicinity of the mouth, nose or upper respiratory tract do not enter the lungs.

4. A method as claimed in claim 1 wherein at least 75% by volume of the airborne respirable particles or droplets having a diameter of less than 10

micrometres in the vicinity of the mouth, nose or upper respiratory tract do not enter the lungs.

5. (Amended) A method as claimed in claim 4 in which the spray device is an aerosol spray device.

6. (Amended) A method as claimed in claim 5 in which the spray device contains an emulsion.

7. (Amended) A method as claimed in claim 6 in which the liquid droplets have a size in the range of from 5 to 100 micrometres.

8. (Amended) A method as claimed in claim 7 in which the spray device contains a composition comprising an oil phase, an aqueous phase, a surfactant and a propellant.

9. A method as claimed in claim 8 wherein the oil phase includes a C₉-C₁₂ hydrocarbon.

10. A method as claimed in claim 9 wherein the C₉-C₁₂ hydrocarbon is present in the composition in an amount of from 2 to 10% w/w.

11. (Amended) A method as claimed in claim 8 wherein the surfactant is glyceryl oleate or a polyglycerol oleate.

12. (Amended) A method as claimed in claim 11 wherein the surfactant is present in the composition in an amount of from 0.1 to 1.0% w/w.

13. (Amended) A method as claimed in claim 8 wherein the propellant is liquified petroleum gas.

14. A method as claimed in claim 13 wherein the propellant is present in the composition in an amount of from 20 to 50% w/w.

15. (Amended) A method as claimed claim 7 wherein the unipolar charge is imparted to the liquid droplets solely by the interaction between the liquid and the spray device, without any charge being imparted thereto from an internal or external charge inducing device.

16. (Amended) A method as claimed in claim 15 wherein the required charge to mass ratio is imparted to the liquid droplets as a result of the use of an aerosol spray device with at least one of the features of:

- (a) the material of the actuator,**
- (b) the size and shape of the orifice of the actuator,**
- (c) the diameter of the dip tube,**
- (d) the characteristics of the valve, and**
- (e) the formulation of the composition contained within the aerosol spray device**

10 being chosen in order to achieve said droplet charge to mass ratio by double layer charging imparting the unipolar charge to the droplets during the actual spraying of the liquid droplets from the orifice of the aerosol spray device.--

Attached is a copy of the amended claims marked to show changes.

In the Abstract:

Attached, as page 22, of the application is an Abstract of the Disclosure.

Applicant : Rodney Thomas FOX
Serial No. : PCT/GB99/01963
Filed : 23 June 1999
Page : 6

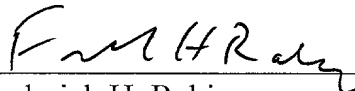
Attorney's Docket No.: 08291-670001

REMARKS

The foregoing Amendment inserts section headings into the specification, corrects some typographical errors, amends the claims to conform to American practice and adds an Abstract complying with 37 C.F.R. § 1.72(b).

Respectfully submitted,

Date: 2 Jan. 2001



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Appendix A

5. (Amended) A method as claimed in [any one of the preceding claims] claim 4 in which the spray device is an aerosol spray device.

6. (Amended) A method as claimed in [any one of the preceding claims] claim 5 in which the spray device contains an emulsion.

7. (Amended) A method as claimed in [any one of the preceding claims] claim 6 in which the liquid droplets have a size in the range of from 5 to 100 micrometres.

8. (Amended) A method as claimed in [any one of the preceding claims] claim 7 in which the spray device contains a composition comprising an oil phase, an aqueous phase, a surfactant and a propellant.

11. (Amended) A method as claimed in [any one of] claim 8 [to 10] wherein the surfactant is glyceryl oleate or a polyglycerol oleate.

12. (Amended) A method as claimed in [any one of claims 8 to] claim 11 wherein the surfactant is present in the composition in an amount of from 0.1 to 1.0% w/w.

13. (Amended) A method as claimed in [any one of claims] claim 8 [to 12] wherein the propellant is liquified petroleum gas.

15. (Amended) A method as claimed [in any one of the preceding claims] claim 7 wherein the unipolar charge is imparted to the liquid droplets solely by the interaction between the liquid and the spray device, without any charge being imparted thereto from an internal or external charge inducing device.

16. (Amended) A method as claimed in claim 15 wherein the required charge to mass ratio [of at least $\pm 1 \times 10^{-4}$ C/kg] is imparted to the liquid droplets as a result of the use of an aerosol spray device with at least one of the features of: (a) the material of the actuator, (b) the size and shape of the orifice of the actuator, (c) the diameter of the dip tube, (d) the characteristics of the valve, and (e) the formulation of the composition contained within the aerosol spray device being chosen in order to achieve [the] said droplet charge to mass ratio by double layer charging imparting the unipolar charge to the droplets during the actual spraying of the liquid droplets from the orifice of the aerosol spray device.--

INHALATION OF AEROSOL ACTIVES

The present invention relates to a method of reducing the inhalation of compositions which are sprayed into the atmosphere, in particular those which are sprayed from an aerosol spray device.

Aerosols spray compositions produce potential health/breathing hazards through the inhalation of the spray particles or droplets. It is known that, for example, so-called PM10 particles (herein defined as those particles with a particle size of less than 10 micrometres) are capable of travelling deep into the respiratory tract. A typical aerosol spray device will produce liquid droplets with a range of droplet diameters, but usually a proportion of the droplets have a droplet diameter of less than 10 micrometres.

We have now developed a method whereby the inhalation of aerosol compositions can be reduced.

According to the present invention there is provided a method of reducing the inhalation of airborne/respirable particles or droplets having a diameter of less than 10 micrometres, produced by spraying liquid droplets from a spray device, which method comprises imparting a unipolar charge to the liquid droplets by double layer charging during the spraying of the droplets from a spray device, the unipolar charge being at a level such that the droplets have a charge to mass ratio of at least $\pm 1 \times 10^{-4}$ C/kg, whereby at least 10% by volume of the airborne respirable particles or droplets having a diameter of less than 10 micrometres in the vicinity

of the mouth, nose or upper respiratory tract do not enter the lungs.

It is preferred that the unipolar charge which is imparted to the liquid droplets is generated solely by the interaction between the liquid within the spray device and the spray device itself as the liquid is sprayed therefrom. In particular, it is preferred that the manner in which a unipolar charge is imparted to the liquid droplets does not rely even partly upon the connection of the spray device to any external charge inducing device, such as an external source of relatively high voltage, or any internal charge inducing device such as a battery. With such an arrangement, the spray device is entirely self-contained making it suitable for use both in industrial, institutional and domestic situations.

Preferably, the spray device is a domestic pressure-spraying device devoid of any electrical circuitry but which is capable of being hand held. Typically such a device has a capacity in the range of from 10ml to 2000ml and can be actuated by hand, or by an automatic actuating mechanism. A particularly preferred domestic device is a hand-held aerosol can.

Preferably, therefore the charge to mass ratio of at least $\pm 1 \times 10^{-4}$ C/kg is imparted to the liquid droplets as a result of the use of an aerosol spray device with at least one of the features of the material of the actuator, the size and shape of the orifice of the actuator, the diameter of the dip tube, the characteristics of the valve and the formulation of the composition contained within the aerosol spray

device being chosen in order to achieve the said droplet charge to mass ratio by double layer charging imparting the unipolar charge to the droplets during the actual spraying of the liquid droplets from the orifice of the aerosol spray device.

As a result of the method of the present invention, the liquid droplets which form the aerosol spray produced by the spray device carry an electrostatic charge. The charged droplets will seek to disperse as a result of mutual repulsion and will preferentially move towards surfaces having an opposite or a neutral charge, such as the face, nose or in the upper respiratory tract, rather than penetrating into the lungs of humans or animals in the vicinity of the aerosol spray. The higher the charge on the liquid droplets which form the aerosol spray, the more readily they will seek to deposit on the mouth, nose or upper respiratory tract. The rate of flow of the liquid product as it is dispensed from the spray device will also have an effect on the amount deposited with lower flow rates encouraging more deposition than higher flow rates.

The method of the present invention has application in connection with all or most aerosol spray devices in current use, examples being paint aerosols, antiperspirants, hair sprays, insecticides, horticultural products, air fresheners, waxes and polishes, oven cleaners, starches and fabric finishes, shoe and leather care products, glass cleaners and various other household, institutional, professional or industrial products.

The method of the present invention prevents at least 10%, preferably at least 25%, and more preferably at least 40%, yet more preferably at least 75% by volume and even more preferably at least 85% by volume of the airborne particles having a size of less than 10 micrometres from entering the lungs.

The airborne particles may either comprise the liquid droplets per se, or may comprise particles which are produced as the droplets break up or evaporate after spraying.

In general, the liquid composition which is sprayed into the air using the spray device is a water and hydrocarbon mixture, or emulsion, or a liquid which is converted into an emulsion by shaking the spraying device before use, or during the spraying process.

While all liquid aerosols are known to carry a net negative or positive charge as a result of double layer charging, or the fragmentation of liquid droplets, the charge imparted to droplets of liquid sprayed from standard devices is only of the order of $\pm 1 \times 10^{-8}$ to 1×10^{-5} C/kg.

The invention relies on combining various characteristics of an aerosol spray device so as to increase the charging of the liquid as it is sprayed from the aerosol spray device.

A typical aerosol spray device comprises:

1. An aerosol can containing the composition to be sprayed from the device and a liquid or gaseous propellant;
2. A dip tube extending into the can, the upper

end of the dip tube being connected to a valve;

3. An actuator situated above the valve which is capable of being depressed in order to operate the valve; and

4. An insert provided in the actuator comprising an orifice from which the composition is sprayed.

A preferred aerosol device for use in the present invention is that described in WO 97/12227.

It is possible to impart higher charges to the liquid droplets by choosing aspects of the aerosol device including the material, shape and dimensions of the actuator, the actuator insert, the valve and the dip tube and the characteristics of the liquid which is to be sprayed, so that the required level of charge is generated as the liquid is dispersed as droplets. A number of characteristics of the aerosol system increase double layer charging and charge exchange between the liquid formulation and the surface of the aerosol system. Such increases are brought about by factors which may increase the turbulence of the flow through the system, and increase the frequency and velocity of contact between the liquid and the internal surface of the container and valve and actuator system.

By way of example, characteristics of the actuator can be optimised to increase the charge levels on the liquid sprayed from the container. A smaller orifice in the actuator insert, of a size of 0.45mm or less, increase the charge levels of the

liquid sprayed through the actuator. The choice of material for the actuator can also increase the charge levels on the liquid sprayed from the device with material such as nylon, polyester, acetal, PVC and polypropylene tending to increase the charge levels. The geometry of the orifice in the insert can be optimised to increase the charge levels on the liquid as it is sprayed through the actuator. Inserts which promote the mechanical break-up of the liquid give better charging.

The actuator insert of the spray device may be formed from a conducting, insulating, semi-conducting or static-dissipative material.

The characteristics of the dip tube can be optimised to increase charge levels in the liquid sprayed from the container. A narrow dip tube, of for example about 1.27mm internal diameter, increases the charge levels on the liquid, and the dip tube material can also be changed to increase charge.

Valve characteristics can be selected which increase the charge to mass ratio of the liquid product as it is sprayed from the container. A small tailpiece orifice in the housing, of about 0.65mm, increases the charge to mass ratio during spraying. A reduced number of holes in the stem, for example 2 x 0.50mm, also increases the charge during spray. The presence of a vapour phase tap helps to maximise the charge levels, a larger orifice vapour phase tap of, for example, about 0.50mm to 1.0mm generally giving higher charge levels.

Changes in the product formulation can also

affect charging levels. A formulation containing a mixture of hydrocarbon and water, or an emulsion of an immiscible hydrocarbon and water, will carry a higher charge to mass ratio when sprayed from the aerosol device than either a water alone or hydrocarbon alone formulation.

It is preferred that a liquid composition of use in the present invention comprises an oil phase, an aqueous phase, a surfactant and a propellant.

10 Preferably the oil phase includes C_9 - C_{12} hydrocarbon which is preferably present in the composition in an amount of from 2 to 10% w/w.

Preferably the surfactant is glyceryl oleate or polyglycerol oleate, preferably present in the composition in an amount of from 0.1 to 1.0% w/w.

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Preferably the propellant is liquified petroleum gas (LPG) which is preferably butane, optionally in admixture with propane. The propellant may be present in an amount of from 10 to 90% w/w depending upon whether the composition is intended for spraying as a "wet" or as a "dry" composition. For a "wet" composition, the propellant is preferably present in an amount of from 20 to 50% w/w, more preferably in an amount of from 30 to 40% w/w.

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The liquid droplets sprayed from the aerosol spray device will generally have diameters in the range of from 5 to 100 micrometres, with a peak of droplets of about 40 micrometres. The liquid which is sprayed from the aerosol spray device may contain a predetermined amount of a particulate material, for example, fumed silica, or a predetermined amount of a

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volatile solid material, such as menthol or naphthalene.

A can for a typical aerosol spray device is formed of aluminium or lacquered or unlacquered tin plate or the like. The actuator insert may be formed
5 of, for instance, acetal resin. The valve stem lateral opening may typically be in the form of two apertures of diameters 0.51mm.

The present invention will now be described, by way of example only, with reference to the
10 accompanying drawings, in which:-

Figure 1 is a diagrammatic cross section through an aerosol spraying apparatus in accordance with the invention;

15 Figure 2 is a diagrammatic cross section through the valve assembly of the apparatus of Figure 1;

Figure 3 is a cross section through the actuator insert of the assembly shown in Figure 2;

Figure 4 shows the configuration of the bore of
20 the spraying head shown in Figure 3 when viewed in the direction A;

Figure 5 shows the configuration of the swirl chamber of the spraying head shown in Figure 3 when viewed in the direction B;

25 Figure 6 illustrates the results obtained in Example 2; and

Figure 7 illustrates the results obtained in Example.

Referring to Figures 1 and 2, an aerosol spray
30 device in accordance with the invention is shown. It comprises a can 1, formed of aluminium or lacquered or

unlacquered tin plate or the like in conventional manner, defining a reservoir 2 for a liquid 3 having a conductivity such that droplets of the liquid can carry an appropriate electrostatic charge. Also

5 located in the can is a gas under pressure which is capable of forcing the liquid 3 out of the can 1 via a conduit system comprising a dip tube 4 and a valve and actuator assembly 5. The dip tube 4 includes one end 6 which terminates at a bottom peripheral part of the

10 can 1 and another end 7 which is connected to a tailpiece 8 of the valve assembly. The tailpiece 8 is secured by a mounting assembly 9 fitted in an opening in the top of the can and includes a lower portion 10 defining a tailpiece orifice 11 to which end 7 of the

15 dip tube 4 is connected. The tailpiece includes a bore 12 of relatively narrow diameter at lower portion 11 and a relatively wider diameter at its upper portion 13. The valve assembly also includes a stem pipe 14 mounted within the bore 12 of the tailpiece

20 and arranged to be axially displaced within the bore 12 against the action of spring 15. The valve stem 14 includes an internal bore 16 having one or more lateral openings (stem holes) 17 (see Figure 2). The valve assembly includes an actuator 18 having a

25 central bore 19 which accommodates the valve stem 14 such that the bore 16 of the stem pipe 14 is in communication with bore 19 of the actuator. A passage 20 in the actuator extending perpendicularly to the bore 19 links the bore 19 with a recess including a

30 post 21 on which is mounted a spraying head in the form of an insert 22 including a bore 23 which is in

communication with the passage 20.

A ring 24 of elastomeric material is provided between the outer surface of the valve stem 14 and, ordinarily, this sealing ring closes the lateral opening 17 in the valve stem 14. The construction of the valve assembly is such that when the actuator 18 is manually depressed, it urges the valve stem 14 downwards against the action of the spring 15 as shown in Figure 2 so that the sealing ring 24 no longer closes the lateral opening 17. In this position, a path is provided from the reservoir 2 to the bore 23 of the spraying head so that liquid can be forced, under the pressure of the gas in the can, to the spraying head via a conduit system comprising the dip tube 4, the tailpiece bore 12, the valve stem bore 16, the actuator bore 19 and the passage 20.

An orifice 27 (not shown in Figure 1) is provided in the wall of the tailpiece 8 and constitutes a vapour phase tap whereby the gas pressure in the reservoir 2 can act directly on the liquid flowing through the valve assembly. This increases the turbulence of the liquid. It has been found that an increased charge is provided if the diameter of the orifice 27 is at least 0.76mm.

Preferably the lateral opening 17 linking the valve stem bore 16 to the tailpiece bore 12 is in the form of 2 orifices each having a diameter of not more than 0.51mm to enhance electrostatic charge generation. Further, the diameter of the dip tube 4 is preferably as small as possible, for example, 1.2mm, in order to increase the charge imparted to the

liquid. Also, charge generation is enhanced if the diameter of the tailpiece orifice 11 is as small as possible eg not more than about 0.64mm.

Referring now to Figure 3, there is shown on an increased scale, a cross section through the actuator insert of the apparatus of Figures 1 and 2. For simplicity, the bore 23 is shown as a single cylindrical aperture in this Figure. However, the bore 23 preferably has the configuration, for instance, shown in Figure 4. The apertures of the bore 23 are denoted by reference numeral 31 and the aperture-defining portions of the bore are denoted by reference numeral 30. The total peripheral length of the aperture-defining portions at the bore outlet is denoted by L (in mm) and a is the total area of the aperture at the bore outlet (in mm^2) and the values for L and a are as indicated in Figure 4. L/a exceeds 8 and this condition has been found to be particularly conducive to charge development because it signifies an increased contact area between the actuator insert and the liquid passing there through.

Many different configurations can be adopted in order to produce a high L/a ratio without the cross-sectional area a being reduced to a value which would allow only low liquid flow rates. Thus, for example it is possible to use actuator insert bore configurations (i) wherein the bore outlet comprises a plurality of segment-like apertures (with or without a central aperture); (ii) wherein the outlet comprises a plurality of sector-like apertures; (iii) wherein the aperture together form an outlet in the form of a

grill or grid; (iv) wherein the outlet is generally cruciform; (v) wherein the apertures together define an outlet in the form of concentric rings; and combinations of these configurations. Particularly preferred are actuator insert bore configurations wherein a tongue like portion protrudes into the liquid flow stream and can be vibrated thereby. This vibrational property may cause turbulent flow and enhanced electrostatic charge separation of the double layer, allowing more charge to move into the bulk of the liquid.

Referring now to Figure 5, there is shown a plan view of one possible configuration of swirl chamber 35 of the actuator insert 22. The swirl chamber includes 4 lateral channels 36 equally spaced and tangential to a central area 37 surrounding the bore 23. In use, the liquid driven from the reservoir 2 by the gas under pressure travels along passage 20 and strikes the channels 36 normal to the longitudinal axis of the channels. The arrangement of the channels is such that the liquid tends to follow a circular motion prior to entering the central area 37 and thence the bore 23. As a consequence, the liquid is subjected to substantial turbulence which enhances the electrostatic charge in the liquid.

The following Examples illustrates the invention:-

EXAMPLE 1

An air freshener formulation was produced as follows:-

5 83% by weight of an iso paraffin solvent was introduced into a mixing vessel and stirred. 0.2% by weight of butyl hydroxy toluene was added to the vessel as a corrosion inhibitor and stirring was continued until a homogenous mixture was obtained.

10 Thereafter, in turn, 5% by weight of polyglycerol oleate emulsifier and 11.8% by weight of a fragrance component were added and stirring was again continued until a homogeneous mixture had been produced.

 The mixture constituted the oil phase of the

15 final product. 6% by weight of this oil phase was placed in a tin plated aerosol can of the type as described with reference to Figures 1 and 2, having a spraying head bore configuration as shown in Figure 4 and a spraying head swirl chamber configuration as

20 shown in Figure 5. The actuator insert was formed of acetal resin.

 The valve stem lateral opening 17 was in the form of 2 apertures of diameter 0.51mm, the vapour phase tap orifice 27 had a diameter of 0.76mm, the

25 tail pipe orifice 11 had a diameter of 0.64mm and the diameter of the dip tube 4 was 3mm. 59% by weight of soft water was then added to the can and thereafter the valve assembly was fitted onto the can. 35% by weight of butane was introduced into the can via the

30 valve assembly to achieve a pressure of 40 psi. On depression of the actuator 18, a fine spray of

liquid droplets having a charge/mass value of -1×10^{-4} C/kg and a flow rate of approximately 1.5 g/sec was obtained. The droplets became rapidly dispersed in the air.

5 The above-described aerosol spray device was compared with a standard, known aerosol spray device loaded with the same air freshener formulation. It was found that, for the same amount of spraying, the quantity of liquid droplets inhaled was significantly
10 less with the above-described device compared with the standard, known device.

EXAMPLE 2

15 A model head with a conducting surface and oral orifice tube was positioned in a booth (2m³) and earthed. Pieces of filter paper (grade 4) sized 1.5cm² were attached to the face at the left of the nose, the right eye and the right side of the mouth.
20 In each test 7g +/- 0.35g of aerosol product was introduced into the booth by a 3 second spray. Aerosol was introduced into the booth from a position of 1.4m behind and 0.25m above the model head. The product used in these tests had the composition given
25 below:

	Ingredient	%w/w
	Bioallethrin	0.241
	Bioresmethrin	0.046
	Butylated hydroxytoluene	0.005
5	Deionised water	51.15
	Fluorescein	0.05
	H55 (26% w/w propane/butane blend (Boral)	40.000
	Norpar 13 (Exxon)	7.500
10	Perfume	0.100
	Polyglycerol oleate	0.900

After spraying, the booth was left for 10 minutes and the filter paper removed.

15 Fluorescein is not very water soluble, and so a phosphate buffer (pH 7, 0.1M $\text{Na}_2\text{HPO}_4 + \text{NaH}_2\text{PO}_4 \cdot \text{H}_2\text{O}$) was used to extract the fluorescein from the filter paper. 5ml of buffer was added to the paper and left for 24 hours. The paper was then removed and the sample

20 tested in a fluorimeter. The fluorimeter was set at zero reading when buffer alone was present in the cuvette. Known concentrations of product were made in phosphate buffer to use as calibration samples. Product was sprayed into a vial and 40mg weighed out.

25 10ml of buffer was added, and 5ml of this was removed and placed in another vial and 5ml of buffer added to get a second concentration of 20mg/10ml. Further dilutions were made in the same way so that

30 concentrations of 10, 5, 2.5, 1.25 and 0.625gm/10ml were obtained. These known concentrations and their

fluorescence readings were then used to find the regression line. The equation of the line was then used to determine how much product was present in the test samples from their fluorescence reading. This value was then divided by the amount of product sprayed in the test to get a value of the amount of product landing on the face per gram of product sprayed and thus removing any effect of a slightly variable spray length.

Charged aerosol was artificially produced by applying - 10kV to the can, since the presence of fluorescein made it difficult to charge the spray naturally. This produced an aerosol with a charge to mass ratio of -4×10^{-4} C/Kg. This was compared with an uncharged aerosol spray of the same composition.

As shown in Figure 6, uncharged sprays deposited a mean of 0.115mg of product/g sprayed ($n=12$, $s=0.064$) on the face papers. Charged sprays deposited 63% more product on the face as compared to uncharged sprays. 0.305mg of product/g sprayed was collected ($n=12$, $s=0.172$). The difference is significant at $P<0.05$ ($t=3.59$, 22df).

EXAMPLE 3

25

Following the procedure described in Example 2 a 3 second spray of the following composition was tested.

30

5

Ingredient	%w/w
Isopar G	4.996
Butylated hydroxytoluene	0.013
Polyglycerol oleate	0.299
Perfume	0.702
Propane/butane blend	58.94
Fluorescein	0.05

10 Charged aerosol was artificially produced by applying - 10kV to the can, which produced an aerosol with a charge to mass ratio of -2.4×10^{-4} C/kg. This was compared with an uncharged aerosol spray of the same composition.

15 As shown in Figure 7, uncharged spray deposits a mean of 0.099mg of product/g sprayed ($s=0.032$) on the face targets. Charged sprays deposited 73.5% more product on the face as compared to uncharged sprays, 0.374 mg of product/g sprayed was collected ($s=0.09$). The difference is significant $P<0.05$ ($t=9.85$, 10df).

20

CLAIMS:

1. A method of reducing the inhalation of airborne/respirable particles or droplets having a diameter of less than 10 micrometres, produced by spraying liquid droplets from a spray device, which method comprises imparting a unipolar charge to the liquid droplets by double layer charging during the spraying of the droplets from a spray device, the unipolar charge being at a level such that the droplets have a charge to mass ratio of at least $\pm 1 \times 10^{-4}$ C/kg, whereby at least 10% by volume of the airborne respirable particles or droplets having a diameter of less than 10 micrometres in the vicinity of the mouth, nose or upper respiratory tract do not enter the lungs.

2. A method as claimed in claim 1 wherein at least 25% by volume of the airborne respirable particles or droplets having a diameter of less than 10 micrometres in the vicinity of the mouth, nose or upper respiratory tract do not enter the lungs.

3. A method as claimed in claim 1 wherein at least 40% by volume of the airborne respirable particles or droplets having a diameter of less than 10 micrometres in the vicinity of the mouth, nose or upper respiratory tract do not enter the lungs.

4. A method as claimed in claim 1 wherein at least 75% by volume of the airborne respirable

particles or droplets having a diameter of less than 10 micrometres in the vicinity of the mouth, nose or upper respiratory tract do not enter the lungs.

5 5. A method as claimed in any one of the preceding claims in which the spray device is an aerosol spray device.

10 6. A method as claimed in any one of the preceding claims in which the spray device contains an emulsion.

15 7. A method as claimed in any one of the preceding claims in which the liquid droplets have a size in the range of from 5 to 100 micrometres.

20 8. A method as claimed in any one of the preceding claims in which the spray device contains a composition comprising an oil phase, an aqueous phase, a surfactant and a propellant.

9. A method as claimed in claim 8 wherein the oil phase includes a C₉ - C₁₂ hydrocarbon.

25 10. A method as claimed in claim 9 wherein the C₉ - C₁₂ hydrocarbon is present in the composition in an amount of from 2 to 10% w/w.

30 11. A method as claimed in any one of claims 8 to 10 wherein the surfactant is glyceryl oleate or a polyglycerol oleate.

12. A method as claimed in any one of claims 8 to 11 wherein the surfactant is present in the composition in an amount of from 0.1 to 1.0% w/w.

5 13. A method as claimed in any one of claims 8 to 12 wherein the propellant is liquified petroleum gas.

10 14. A method as claimed in claim 13 wherein the propellant is present in the composition in an amount of from 20 to 50% w/w.

15 15. A method as claimed in any one of the preceding claims wherein the unipolar charge is imparted to the liquid droplets solely by the interaction between the liquid and the spray device, without any charge being imparted thereto from an internal or external charge inducing device.

20 16. A method as claimed in claim 15 wherein the charge to mass ratio of at least $\pm 1 \times 10^{-4}$ C/kg is imparted to the liquid droplets as a result of the use of an aerosol spray device with at least one of the features of the material of the actuator, the size and
25 shape of the orifice of the actuator, the diameter of the dip tube, the characteristics of the valve and the formulation of the composition contained within the aerosol spray device being chosen in order to achieve the said droplet charge to mass ratio by double layer
30 charging imparting the unipolar charge to the droplets during the actual spraying of the liquid droplets from

the orifice of the aerosol spray device.

Abstract

A method of reducing the inhalation of airborne/respirable particles or droplets having a diameter of less than 10 micrometres, produced by spraying liquid droplets from a spray device, which method comprises imparting a
5 unipolar charge to the liquid droplets by double layer charging during the spraying of the droplets have a charge to mass ratio of at least $\pm 1 \times 10^{-4}$ C/kg, whereby at least 10% by volume of the airborne respirable particles or droplets having a diameter of less than 10 micrometres in the vicinity of the mouth, nose or upper respiratory tract do not enter the lungs.

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This diagram illustrates a medical device, possibly a catheter or a probe, designed for insertion into a container (1). The device features a main shaft (7) that transitions into a flexible section (4) and terminates in a distal tip (6). The tip is encased within a sheath (5). A complex control mechanism is located at the proximal end of the shaft, involving a series of components including a handle (20), a control rod (18), and a series of internal and external seals and guides (14, 16, 19, 21, 22, 23, 24). The device is shown inserted into a container (1) which contains a liquid (3). The container has a top opening (2) and a series of horizontal lines indicating the liquid level. The diagram is labeled with various numbers (1-24) corresponding to specific parts of the device and container.

FIG. 2.

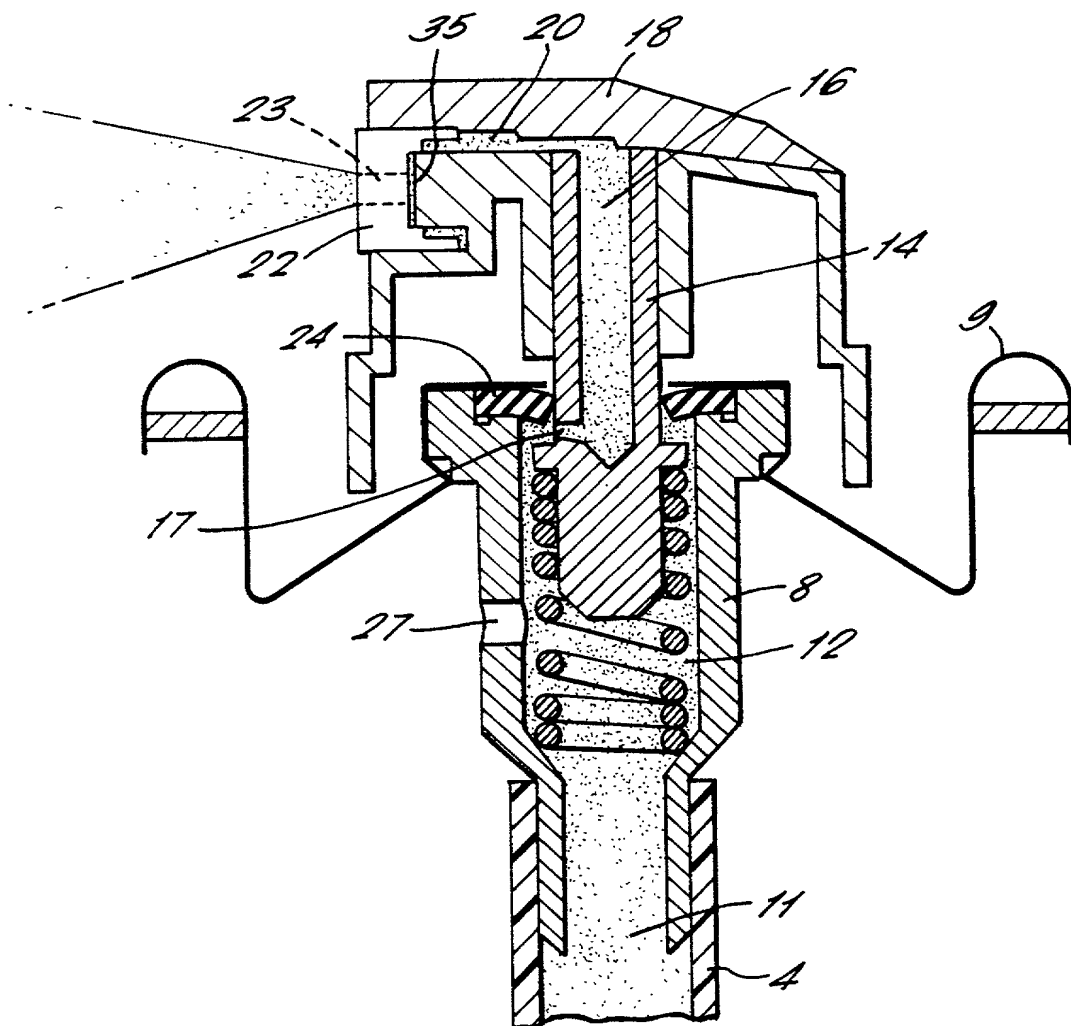


FIG. 3.

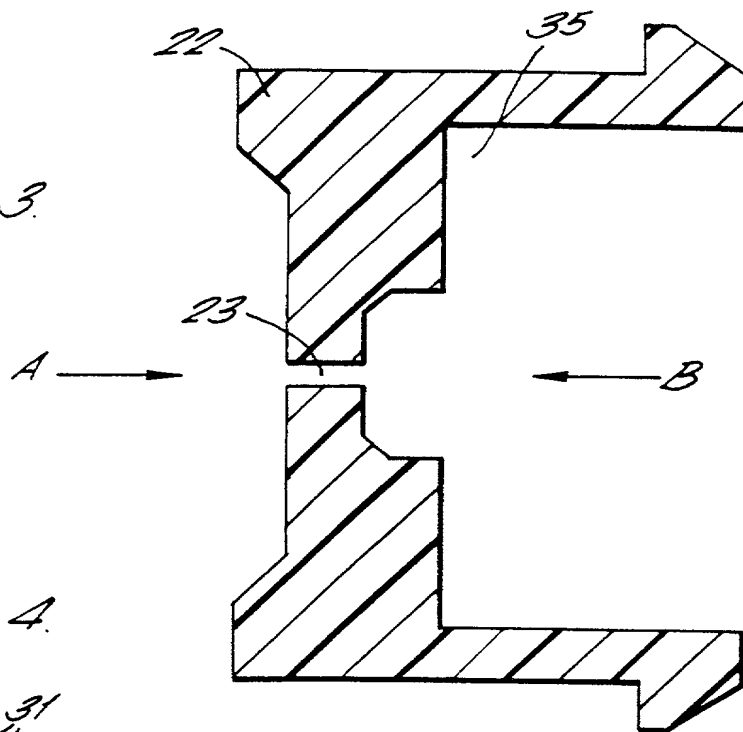


FIG. 4.

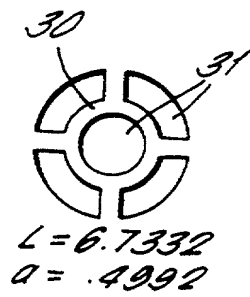


FIG. 5.

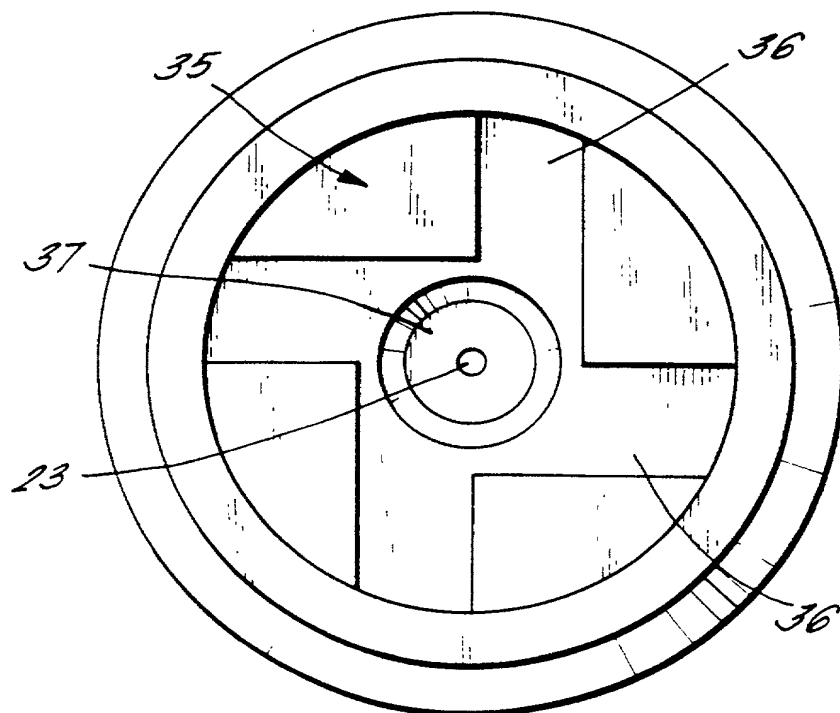


FIG. 6.

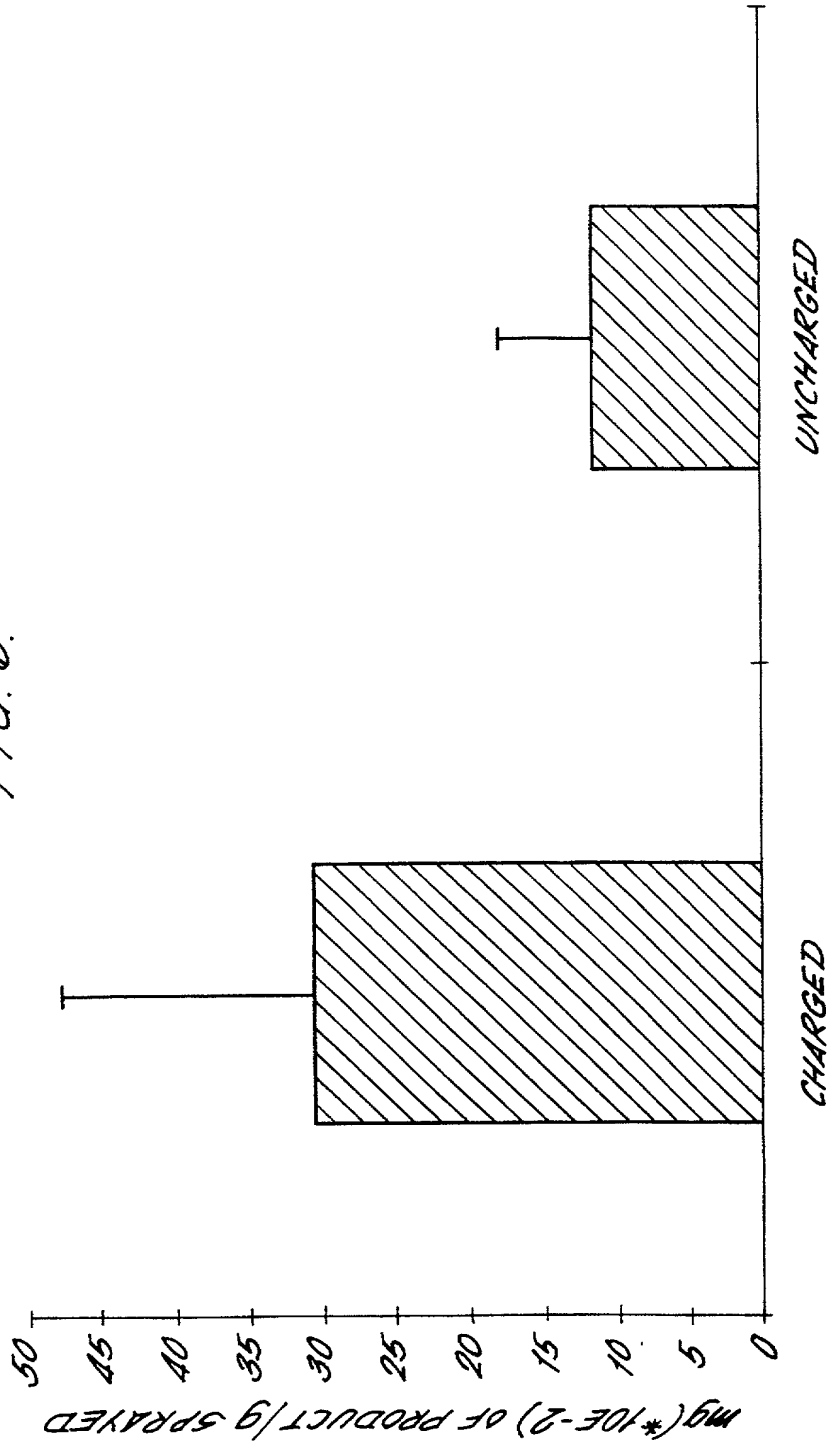
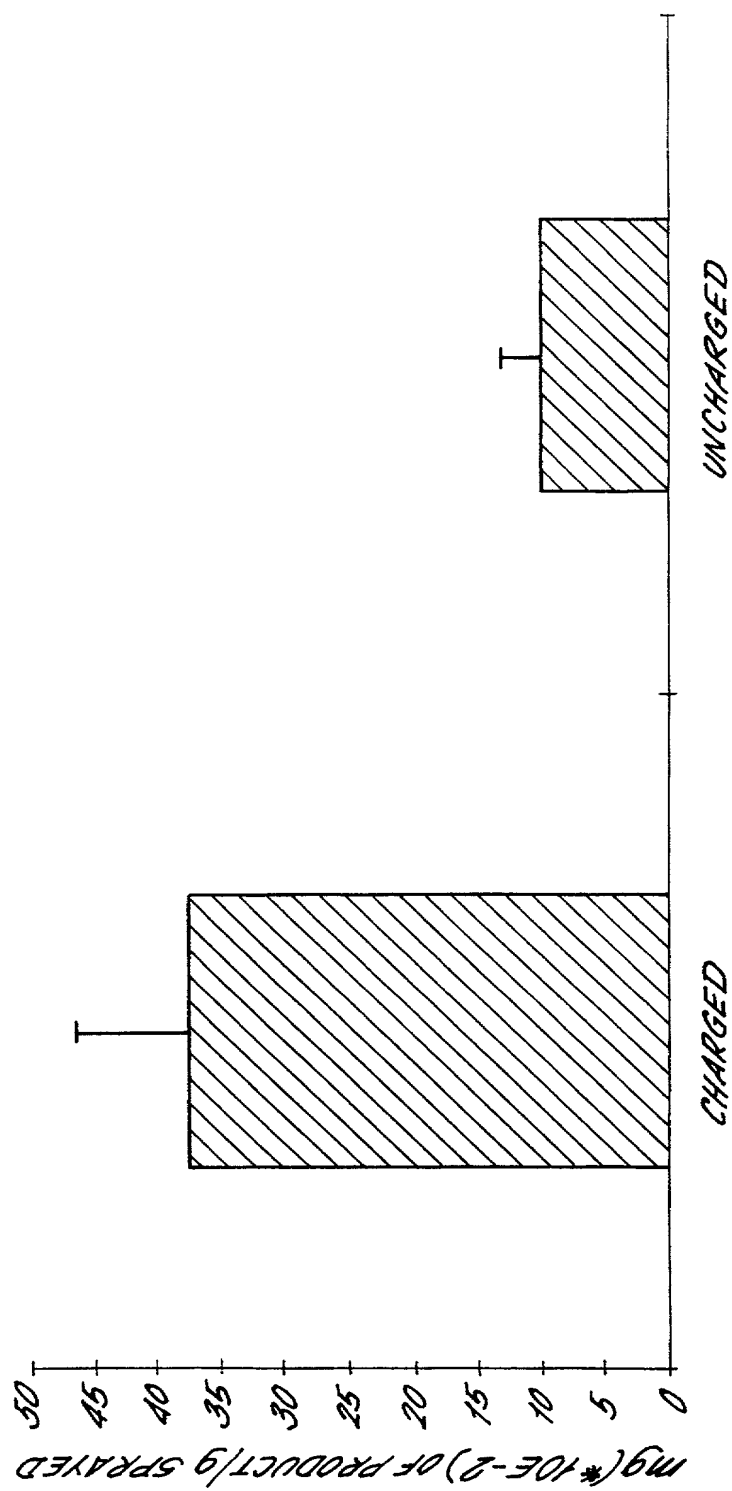


FIG. 7.



COMBINED DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled INHALATION OF AEROSOL ACTIVES, the specification of which:

- ☐ is attached hereto.
☐ was filed on _ as Application Serial No. _ and was amended on _____.
☒ was described and claimed in PCT International Application No. PCT/GB99/01963
filed on 23 June 1999 and as amended under PCT Article 19 on _____.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose all information I know to be material to patentability in accordance with Title 37, Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

Country	Application No.	Filing Date	Priority Claimed
United Kingdom	9814368.8	2 July 1998	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

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1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

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